Section II. (REMARKS)

The pending claims are 1-4, 6-8, 19, 26, 28, 29, 31, and 35-40.

Claims 1, 2, 4, 6-8, 19, 26, 28 and 29 have been amended herein, without prejudice. Claims 5, 9, 18, 30, and 32-34 have been cancelled herein, without prejudice, and with the reservation of the right to file said claims and related subject matter in continuing and/or divisional applications.

Claims 35-40 are new.

No new matter has been added herein.

Allowable Subject Matter

According to the Examiner, claim 31 is allowed and claims 2, 19, 26 and 28-29 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants acknowledge same.

In addition, the Examiner has indicated that the prior art of record does not disclose or suggest the structure of SEQ ID NO: 17. Accordingly, the claims relating to SEQ ID NO: 17 should be allowable.

Rejection of Claims and Transversal Thereof

In the March 13, 2009 Office Action:

- claims 1, 3-9, 18, 30 and 32-34 were rejected under 35 U.S.C. §112, first paragraph; and
- claims 5-9 were rejected under 35 U.S.C. §112, second paragraph.

These rejections are respectfully traversed. The patentable distinctions of the pending claims over the cited references are set out in the ensuing discussion.

Rejections under 35 U.S.C. §112, first paragraph

In the March 13, 2009 Office Action, claims 1, 3-9, 18, 30 and 32-34 were rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. Applicants traverse such rejection.

1. According to the Examiner, there is no basis for the phrase "between 9 and 14 amino acid residues" in claim 1. Applicants vigorously disagree.

Claim 1 has been amended to recite:

> **"A peptide comprising an amino acid sequence which contains SEQ ID NO: 17 or between 9, 10, 11, 12, 13, or 14 consecutive amino acid residues of SEQ ID NO:17 starting from the first amino acid residue of the amino terminal end of SEQ ID NO: 17, and their pharmaceutically acceptable salts, wherein the peptide is characterized by a capacity to bind to transforming growth factor β1 (TGF-β1)."** (emphasis showing added limitation(s))

Support for the amendment to claim 1 includes the instant specification at page 6, lines 21-28 and Example 4. Applicants disclosed at page 6, lines 21-28 that the peptide can comprise 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 consecutive amino acids of SEQ ID NO: 17 and Example 4 relates to the specific truncation of SEQ ID NO: 17 whereby SEQ ID NOS: 33-36 represent p17 (1-14), p17 (1-12), p17 (1-10) and p17 (1-9), respectively.

According to the MPEP, the test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Further, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice. It is clear referring to Example 4 that applicants were in possession of a representative number of species of the claimed amino acid sequence selected from 9, 10, 11, 12, 13, or 14 consecutive amino acid residues of SEQ ID NO:17 starting from the first amino acid residue of the amino terminal end of SEQ ID NO: 17, wherein the peptide is characterized by a capacity to bind to transforming growth factor β1 (TGF-β1). Accordingly, applicants' claim 1 satisfies the written description requirement.

Applicants have cancelled claims 9, 33 and 34, without prejudice, and as such, the rejection of same is

moot.

Withdrawal of the rejection of claims 1, 3-9, 18, 30 and 32-34 for lacking written description is respectfully requested.

2. According to the Examiner, claims 5-7 fail to comply with the enablement requirement. Specifically, the Examiner indicated that the specification does not enable producing pharmaceutical compositions for the treatment of diseases and pathological alterations associated with excessive or deregulated expression of TGF-β1. Applicants vigorously disagree.

It is well established in the law that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. It has been consistently held that the first paragraph of 35 U.S.C. §112 does not require explaining every detail since the inventor is speaking to those skilled in the art. Further, applicants remind the Examiner that some experimentation may be required as long as it is not undue. In *PPG Indus., Inc., v. Guardian Indus. Corp.*, 27 USPQ2d 1618, 1623 (Fed. Cir. 1996), the court stated that even where some experimentation is necessary to reduce an invention to practice, the enablement requirement is satisfied where: (1) the experimentation is routine; or (2) the specification provides "a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention." As will be discussed below, applicants' specification meets these requirements.

Example 3 of the instant specification discloses the antifibrotic effect of SEQ ID NO: 17 on the inhibition of *in vivo* TGF-β1 biological activity in rats having acute liver damage induced by CCl_4 (the CCl_4 produces cirrhosis with a marked liver fibrosis). The SEQ ID NO: 17 peptide inhibited the biological activity of TGF-β1 *in vivo* by 93% relative to the control.

Example 4 of the instant specification discloses the effect of the truncated peptides of SEQ ID NO: 17 (i.e., p17 (1-14), p17 (1-12), p17 (1-10) and p17 (1-9)) relative to SEQ ID NO: 17 on the *in vitro* TGF-β1 biological activity as calculated from the Mv-1-Lu cell line growth reestablishment assay. It can be seen that the percent inhibition of the biological activity of TGF-β1 in the presence of SEQ ID NOs: 17, 33 (p17 (1-14)) and 34 (p17 (1-12)) was comparable, which evidences that the N-terminal is preferably

conserved.[1] Considering Examples 3 and 4 simultaneously, one skilled in the art would immediately recognize that the N-terminal end of SEQ ID NO: 17 is the active end of the peptide and the conservation of that N-terminal end results in a peptide that inhibits the biological activity of TGF-β1 *in vitro* similar to SEQ ID NO: 17, should be an effective inhibitor *in vivo* as well. Accordingly, applicants have provided a specification that provides "a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention." Accordingly, the specification does enable the practice of claims 5-7 by one skilled in the art.

Considered *in toto*, applicants request withdrawal of the rejection of claims 1, 3-9, 18, 30 and 32-34 under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §112, second paragraph

In the March 15, 2009 Office Action, claims 5-9 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse such rejection.

1. According to the Examiner, claims 5-7 do not provide further limitations to the steps for making the pharmaceutical composition. Applicants have amended claim 4 to include the language of previously pending claim 5 thereby obviating this rejection. Claims 6 and 7 have been amended to depend from claim 4.

2. According to the Examiner, claim 8 is indefinite because of the use of the phrase "therapeutically effective amount." Applicants vigorously disagree.

Claim 8 has been amended to remove the term "therapeutically." The CCPA previously stated that "effective amount" is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation. *In re Halleck*, 164 USPQ 647 (CCPA 1970). In the present case, one skilled in the art would be able to determine the specific amount of peptide needed in the

[1] The removal of lysine (K) from the N-terminal end implies a loss of activity of peptide SEQ ID NO: 17 from 28.5% to 9.4%. In contrast, the removal of at least three amino acids from the C-terminal end does not affect the activity of the peptide.

pharmaceutical composition without undue experimentation.

3. According to the Examiner, claim 9 is indefinite because of the term "alternative." Applicants have cancelled claim 9 and as such, this rejection is moot.

Considered *in toto*, applicants request withdrawal of the rejection of claims 5-9 under 35 U.S.C. §112, second paragraph.

Fees Payable

Six (6) claims have been added, one (1) of which is independent, and seven (7) claims have been cancelled herein, bringing the total number of pending claims to eighteen (18), three (3) of which are independent. As such, no added claims fee is due at this time.

Authorization is hereby given to charge any deficiency in applicable fees for this response to Deposit Account No. 13-4365 of Moore & Van Allen PLLC.

Conclusion

Based on the foregoing, claims 1-4, 6-8, 19, 26, 28, 29, 31, and 35-40 are in form and condition for allowance. If any additional issues remain, the Examiner is requested to contact the undersigned attorney at (919) 286-8000 to discuss same.

Respectfully submitted,

MOORE & VAN ALLEN PLLC

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By: _____

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